## REMARKS

### 1. Interview Conducted on 16 October 2003

Applicants wish to express their appreciation for the helpfulness and attention of Examiners Yaen and Nichol to Applicants' representative and the undersigned during the interview of October 16, 2003. As set forth in the Interview Summary Record, the rejections of record were discussed with respect to the claims, including declaration evidence on clinical trials and a certified English translation of Applicants' priority document to overcome the prior art rejections.

### 2. Objection Under 35 U.S.C. 112, First Paragraph

Claim 6 has been rejected under 35 U.S.C. 112, first paragraph for allegedly lacking enablement. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Page 2 of the Office Action explains that this rejection is based on the Examiner's opinion that "the specification has not taught how to use the composition wherein there are two or more antibodies". From discussions during the interview, it appears that the real basis of the rejection is whether the specification sufficiently enables the use of more than just the HE2 antibody described in the present specification. But regardless of the specific reason for the rejection, Applicants submit that the specification fully enables the use of other antibodies besides the HE2 antibody, and fully enables the use of a composition wherein there are two or more antibodies.

#### 2.1 Brief Explanation of the Invention

The present invention relates to the treatment of cancer by use of an antibody directed against the cellular membrane antigen Ep-CAM. Applicants have found that administration of such an antibody induces an immune response by the patient's own body against carcinoma cells. Enclosed as Exhibit 1 is a copy of a brochure which was also provided to the Examiner during the interview and that describes the clinical trials with Applicants' product IGN101 (comprising the murine monoclonal antibody 17-1A) together with a vaccine adjuvant. The first section on page 2 of the brochure entitled "Mode of Action" explains and schematically illustrates how administration of IGN101 induces production by the patient of antibodies that destroy Ep-CAM positive tumor cells.

**2.2 Response to Rejection**

The present invention is broadly directed to the use of antibodies directed against a tumor-associated antigen (TAA) for the treatment of cancer, particularly the use of antibodies against the TAA known as Ep-CAM (see the paragraph bridging pages 3 and 4 through the first full paragraph of the specification). Monoclonal antibodies against various tumor-associated antigens, including EpCAM, were *per se* known and available to those skilled in the art at the time of the present invention (see page 4, lines 17-18).

The present application describes that various types of antibodies can be prepared according to a procedures that were *per se* known in the art (see paragraph bridging pages 4 and 5 of the application) and specifically describes the use of the murine monoclonal antibody HE-2 and the known Ep-CAM antibody KS1-4 (see paragraph bridging pages 4 and 5 of the application and the first full paragraph on page 11 of the application).

However, other Ep-CAM antibodies were *per se* known to those skilled in the art as shown, for example, by the publications listed on enclosed Exhibit 2, a copy of each of the publications also being enclosed herewith.

The present application specifically describes studies utilizing the Ep-CAM antibodies HE2 and KS1-4, but one skilled in the art would be able, with the teaching of the present application, to utilize other Ep-CAM antibodies, such as those described in the publications set forth in Exhibit 2 or other antibodies which could be prepared by procedures that were *per se* well known to those skilled in the art.

With respect to the Examiner's stated objection in the Office Action that the specification does not teach how to use "the composition wherein there are two or more antibodies", Applicants submit that it would be well within the skill of one in the art (with the teachings of the present application) to prepare and utilize a composition containing two antibodies as compared to a composition containing only one antibody. The usefulness of a composition containing two antibodies is further established by the test results reported in the Declaration of Dr. Hans Loibner dated 17 July 2002 and enclosed as Exhibit 3. In essence, the results reported in that Declaration show that animals immunized with two different antibody preparations showed an immune response specific for Ep-CAM.

For the above reasons, Applicants submit that the present specification is indeed sufficiently enabling for the invention defined by claim 6, so that the rejection of that claim should be withdrawn.

**3. Rejection of Claims 1-9 Under 35 U.S.C. 112, First Paragraph**

The Examiner has also rejected claims 1-9 and claims 10-14 under 35 U.S.C. 112, first paragraph. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner basically urges that the specification "has not enabled a vaccine" and that there "is no indication from the specification that the administration of an antibody composition to a subject would indeed 'prevent' the formation of cancer".

It is first of all noted that independent claim 1 is now directed to "a pharmaceutical composition for treatment of cancer disease" and that method claim 8 is directed to "a method of treating cancer disease"; thereby rendering moot the issue about the use of the term "vaccine". Applicants submit that the use of the term "vaccine" is fully supported by the specification, but the claims have been amended to remove this issue so as to expedite prosecution towards allowance of the claims.

To further evidence the usefulness of the invention, the Applicants submit a second Declaration of Dr. Loibner under 37 C.F.R. 1.132, that Declaration being dated 9 September 2003 and enclosed as Exhibit 4. This Loibner Declaration specifically reports the results of clinical trials utilizing the Applicants' product IGN101 that comprises the murine monoclonal antibody 17-1A. That antibody was *per se* known to those skilled in the art and available to those skilled in the art at the time of the present application as evidenced by several of the publications set forth in Exhibit 2. The test results reported in the Exhibit 4 Loibner Declaration show that administration of IGN101 indeed elicited an immune response resulting in antibodies directed against Ep-CAM, clinically resulting in a significant decrease in the number of Ep-CAM positive tumor cells and importantly showing a stabilization of the disease in 15 out of 18 patients for at least two months (see the results reported on page 3 of the Declaration). Efficacy of the treatment is further shown by the results of the phase 2 studies that, as presented on pages 4 and 5 of the Declaration, show the statistically significantly increased survival rates for those patients treated according to the present invention.

Accordingly, reconsideration and withdrawal of the rejection are requested.

**4. Prior Art Rejections**

Claims 1-3 have been rejected under 35 U.S.C. 102(a) over Braun et al. and claim 7 has been rejected under 35 U.S.C. 103(a) over Braun et al. in view of Pardoll D. These rejections are respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Braun et al. reference was published in December, 1999; whereas, the present application is entitled to the earlier priority of its Swiss priority application which was filed on January 13, 1999. In order to perfect the claim to priority and to antedate the Braun et al. reference, enclosed as Exhibit 5 is a sworn English translation of the Swiss priority application. Since the Braun et al. reference is the only reference alleged to anticipate the present invention and is the primary reference for the Examiner's obviousness rejection, antedating the Braun et al. reference overcomes both of the prior art rejections. Reconsideration and withdrawal of those rejections are, therefore, requested.

**SUMMARY**

In summary, Applicants have overcome the only prior art rejections by removing the Braun et al. reference as statutory prior art and Applicants have shown that the claims are indeed fully enabled within the meaning of 35 U.S.C. 112, first paragraph. Applicants submit that the remaining rejections should, therefore, be withdrawn and that all of the claims are now in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson (Reg. No. 30,330) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), the Applicant respectfully petitions for a two (2) month extension of time for filing a response in connection with the present application and the required fee of $210.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

BY _____
Leonard R. Svensson, #30,330

P.O. Box 747
Falls Church, VA 22040-0747
(714) 708-8555

LRS/lmt
0147-0229P

Attachment(s)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on: October 31, 2003
(Date of Deposit)

BIRCH, STEWART, KOLASCH & BIRCH, LLP

Lori M. Hill
(Signature)

October 31, 2003
(Date of Signature)